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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

S.M. SM.

Office Action Summary	Application No.	Applicant(s)	
	09/868,123	COLLINS ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 October 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-47* is/are pending in the application.

4a) Of the above claim(s) *1-22,24-27 and 32-38* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23,28-31 and 39-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2001* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Status of Application, Amendments and/or Claims

Applicant's election (09 October 2003) of Group V (claims 23, 28-31 and 39-47), polynucleotide sequence SEQ ID NO:3 and polypeptide sequence SEQ ID NO:4 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 23, 28-31 and 39-47 are under examination. Claims 1-22, 24-27, 32-38 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Group, there being no allowable generic or linking claim. Election was made **without** traverse 09 October 2003.

Information Disclosure Statement

The references in the IDS submitted 11 February 2003 and 09 May 2002 have not been located. Regretfully, the references listed cannot be considered at this time. Applicants are invited to cite a particular reference(s) that they want to be considered.

Drawings

Figure 2 appears to missing from the instant specification. Figure 2 is required in reply to the Office action to avoid abandonment of the application. The objection to the drawings will not be held in abeyance. No new matter may be entered.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23, 28, 31, 44 and 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 23, 28, 31, 44 and 47 are indefinite because they depend from claims drawn to a non-elected group. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form.

Claim 23 is indefinite because the claim recites "therapeutically effective amount" without the recitation of a condition or disease. The metes and bounds of therapeutically effective amount cannot be determined.

Claims 31 are lack antecedent basis. In claim 31, it is unclear if "said condition" is atopy, allergic condition, asthma or an immune complex disease.

Claims 44 and 47 are indefinite because they are improper multiple dependent claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 23 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of **binding IL-13 to IL-13bc (SEQ ID NO:4)** in a mammalian subject, said method comprising administering a therapeutically effective amount of a pharmaceutical composition comprising **IL-13bc, wherein IL-13bc comprises SEQ ID NO:4** and a pharmaceutically acceptable carrier,

does not reasonably provide enablement for:

a method of **inhibiting binding of IL-13 to the IL-13 receptor** in a mammalian subject, said method comprising administering a therapeutically effective amount of a pharmaceutical composition comprising a protein, wherein the protein comprises **SEQ ID NO:4 from amino acids 26-341 or SEQ ID NO:4 from amino acids 363-380** and a pharmaceutically acceptable carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The specification states that IL-13 exhibits certain biological activities by interacting with an IL-13 receptor on the surface of target cells. IL-13 receptor and IL-4 receptor share a common component which is required for activation. The specification states that because IL-13 does not bind to cells transfected with IL-4 receptor, IL-13 receptor must contain at least one other ligand binding chain (specification, page 2, lines 7-12). The specification teaches the cloning of murine IL-13 binding chain (SEQ ID NO:2) and human IL-13 binding chain (SEQ ID NO:4)(specification page 7, line 29-page 8, line 5). The instant specification discloses *in vitro* experiments which demonstrate the

direct binding of soluble IL-13bc to IL-13 (Example 3) and the binding of IL-13 expressed in COS cells to labeled IL-13bc-Ig fusion protein (Example 4). These experiments, however, are not tantamount to inhibition of binding of IL-13 to the IL-13 receptor *in vivo*. The experiments never demonstrate the binding of IL-13 to the IL-13 receptor and then the inhibition of this binding in the presence of IL-13bc.

Furthermore, the instant experiments only employ the full length protein. There is no description of fragments of SEQ ID NO:4 that exist, while still maintaining function (binding IL-13). The specification provides little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (deletions), and the nature and extent of changes that can be made in these positions. The specification provides no working example of any fragment sequence which would be within the instant claims. As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to significantly alter its functional properties. It is in no way predictable that disclosed fragment sequences would afford a protein having activity comparable to the one disclosed.

Due to the large quantity of experimentation necessary to generate the fragments recited in the claims and screen same for IL-13 receptor binding chain activity and the large quantity of experimentation necessary to demonstrate inhibition of IL-13 to the IL-13 receptor *in vivo*, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence

of working examples directed to same, the complex nature of the invention, and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 28-31 and 39-44 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

a method of treating **allergen-induced airway hyper responsiveness (AHR)** in a mammalian subject, comprising administering a therapeutically effective amount of a pharmaceutical composition comprising **IL-13bc, wherein IL-13bc comprises SEQ ID NO:4 (OR composition comprising an IL-13 antagonist, wherein IL-13 antagonist is IL-13bc protein, comprising SEQ ID NO:4;** relates to claims 30-44) and a pharmaceutically acceptable carrier,

does not reasonably provide enablement for:

a method of treating an **IL-13 related condition** comprising administering a therapeutically effective amount of a pharmaceutical composition comprising **an IL-13 antagonist** and a pharmaceutical acceptable carrier (**OR a protein comprising SEQ ID NO:4 from amino acids 26-341 or SEQ ID NO:4 from amino acids 363-380 or fragments, antibody, mutants, small molecules, etc; IL-13 antagonists as recited in claim 43)** and a pharmaceutically acceptable carrier. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The scope of patent protection sought by Applicant as defined by the claims fails to bear a reasonable correlation with the scope of enabling disclosure set forth in the specification for the following reasons. The specification teaches the reversal of AHR in mice after the administration of IL-13bc (SEQ ID NO:3) (specification, page 28, lines 20-page 29, line 11). The instant claims, however encompass the treatment of any IL-13 related conditions and the administration of any IL-13 antagonist. The specification has not taught how to treat any IL-13 related conditions or the administration of any IL-13 antagonists. IL-13 related conditions encompass diverse conditions such as atopy, asthma, immune complex disease, Grave's disease and lupus and involves many factors such as genetics, environment and diet. The specification establishes no connection between any of these diverse conditions and the instant invention (IL-13bc). In addition, the instant specification teaches that AHR is *not* dependent upon IgE production (page 29, lines 22-25).

Lastly, the instant experiments only employ the full length protein. There is no description of fragments of SEQ ID NO:4, that exist, while still maintaining function (binding IL-13). The specification provides little or no guidance beyond the mere presentation of sequence data to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (deletions), and the nature and extent of changes that can be made in these positions. The specification provides no working example of any fragment sequence which would be within the instant claims. As is well recognized in the art, any modification (even a "conservative" substitution) to a critical structural region of a protein is likely to

significantly alter its functional properties. It is in no way predictable that disclosed fragment sequences would afford a protein having activity comparable to the one disclosed. Furthermore, the instant specification teaches the administration of IL-13bc protein (SEQ ID NO:3) to treat AHR, not *any* IL-13 antagonist. The specification provides little or no guidance beyond the presentation of "IL-13 antagonist" to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (deletions, mutations), and the nature and extent of changes that can be made in these positions. The specification provides little guidance on the types of small molecules that can be employed as IL-13 antagonist. The specification provides no working example of any IL-13 antagonist which would be within the instant claims. The specification fails to disclose that antibodies, mutants, small molecules as recited have IL-13 antagonist activity.

Due to the large quantity of experimentation necessary to treat any type of IL-13 related condition and administer any IL-13 antagonist, the large quantity of experimentation necessary to generate SEQ ID NO:4 fragments or any IL-13 antagonists as recited in the claims and screen same for activity, the lack of direction/guidance presented in the specification regarding which structural features are required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, and the state of the prior art which establishes the unpredictability of the effects of mutation on protein structure and function, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 45-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The instant claims are drawn to a method of inhibiting the interaction of IL-13 with an IL-13bc protein in a mammalian subject, said method comprising administering a therapeutically effective amount of a composition comprising an IL-13 antagonist and a pharmaceutically acceptable carrier. The instant specification teaches *in vitro* experiments which demonstrate the direct binding of soluble IL-13bc to IL-13 (Example 3) and the binding of IL-13 expressed in COS cells to labeled IL-13bc-Ig fusion protein (Example 4). The experiments employed in the instant specification (Examples 3 and 4) are not tantamount to *in vivo* inhibition of IL-13 and IL-13bc binding in the presence of an IL-13 antagonist. The experiments never demonstrate the binding of IL-13 to IL-13bc and then the inhibition of this binding in the presence of any protein, antibody or small molecule or fragment thereof.

In addition, the specification fails to teach how to make any IL-13 antagonist including antibodies, mutants, and small molecules. The specification provides little or no guidance beyond the presentation of "IL-13 antagonist" to enable one of ordinary skill in the art to determine, without undue experimentation, the positions in the protein which are tolerant to change (deletions, mutations), and the nature and extent of

changes that can be made in these positions. The specification provides little guidance on the types of small molecules that can be employed as IL-13 antagonist. The specification provides no working example of any IL-13 antagonist which would be within the instant claims. The specification fails to disclose that antibodies, mutants, small molecules as recited have IL-13 antagonist activity.

Due to the large quantity of experimentation necessary to demonstrate the inhibition of IL-13 with IL-13bc in the presence of any IL-13 antagonist *in vivo* and the large quantity of experimentation necessary to make any IL-13 antagonist, the lack of direction/guidance presented in the specification regarding same, the absence of working examples directed to same, the complex nature of the invention, and the breadth of the claims which fail to recite any parameters regarding IL-13/IL-13bc binding *in vivo* and IL-13 antagonists, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

Claims 39-46 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The specification provides adequate written description for SEQ ID NO:4 but not binding fragments, mutants and small molecules. The instant claims are directed to an IL-13 binding fragments thereof, IL-13bc binding fragments thereof, IL-13Rα1 binding fragment thereof, small molecule capable of inhibiting the interaction of IL- 13 with

IL- 13bc or the interaction of IL-13 with IL-13Rα1. None of these sequences meet the written description provision of 35 USC 112, first paragraph. Thus, the specification provides insufficient written description to support the genus of IL-13 antagonists encompassed by the claim.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

With the exception of SEQ ID NO:4, the skilled artisan cannot envision the detailed chemical structure of the encompassed polypeptides, polynucleotides, and molecules and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See Fiers v. Revel, 25 USPQ2d 1601 at 1606 (CAFC 1993) and Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481 at 1483. In Fiddes, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only isolated polypeptides comprising the amino acid sequence set forth in SEQ ID NO:4, but not the full breadth of the claim meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Regina M. DeBerry whose telephone number is (703) 305-6915. The examiner can normally be reached on 9:00 a.m.-6:00 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on (703) 308-4623. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

RMD
January 12, 2004

GARY KUNZ
SUPERVISORY PATENT EXAMINER
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